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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/574,545	04/05/2006	Enrico Anthony Antonini	1679 WO/US	4059
Jeffrey S Boone Mallinckrodt Inc 675 McDonnell Boulevard PO Box 5840 St Louis, MO 63134				
7590 07/28/2009				
EXAMINER				
CHANDRAKUMAR, NIZAL S				
ART UNIT		PAPER NUMBER		
1625				
MAIL DATE		DELIVERY MODE		
07/28/2009		PAPER		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/574,545

**Applicant(s)**

ANTONINI, ENRICO ANTHONY

**Examiner**

NIZAL S. CHANDRAKUMAR

**Art Unit**

1625

**Period for Reply** -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 13 July 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,2,4-6 and 8-26 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,2,4-6, 8-26 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-8508)
- Paper No(s)/Mail Date \_\_\_\_\_

- 4) ☐ Interview Summary (PTO-413)
- Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 07/13/2009 has been entered.

Claims 1, 3-6, 8-26 are pending.

Previously presented Rejections:

1. Obviousness Rejection over US 4317903
2. Obviousness Rejection over US 4234684, US 4293489, US 4336333, US 4904590 and US 5780589.
3. Double Patenting Rejection

### **Response to applicants Remarks:**

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious

at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Previously presented rejection of claims 1, 3-6, 8-26 as being obvious over the teachings of US 4317903, US 4234684, US 4293489, US 4336333, US 4904590 and US 5780589 is maintained for reasons of record. Applicant's arguments were fully considered but are not persuasive.

Applicant's arguments center mainly on:

a) Claimed subject matter as being different from the subject matter of cited prior art

b) Affidavit of inventor not being given enough weight

Applicants generally reiterate the previously presented arguments. As such the previously presented Examiner's responses apply equally to applicants instant remarks.

Applicant state that the claimed subject matter of process of purification of fentanyl sample containing fentanyl and phenethyl piperaniline is in contrast to the claimed subject matters of the cited references. This is basis of all arguments of the applicant. Applicant argues that the instant claim limitations, i.e., compound to be purified fentanyl, the impurity phenylpiperaniline, the concentration of the impurity in purified product, eluant, loading ratio, column size, pH of the eluant, recycling, etc are not taught, suggested, or disclosed in any of the cited references. As such, applicant state that the office continues to provide inadequate explanation regarding why one of ordinary skill in the art, looking to develop a **new** way of purifying fentanyl on a industrial

scale, would look to the method disclosed by the instant inventor and the office continues to engage in hindsight reconstruction.

Examiner's Response:

The rejection is not anticipatory under 35 U.S.C. 102. As previously stated, the obviousness rejection is based on the obviousness of the 'process of purification' at the time of the instant application. Thus it is not the compounds or the impurity or any of the claim limitations specifically recited in the instant claims. Examiner agrees that the various references cited each teach hplc purification process for **different** compounds with **different** process limitations and steps. The issue at hand is the process of purification of organic compounds by reverse-phase hplc methods by a chemistry laboratory technician at the time of the instant application. It is well known, that most, if not, all organic reactions result in some impurity, side products or unreacted starting material (as in the instant case 'phenethylpiperaniline' starting material used for making fentanyl). Organic chemists use chromatographic methods as **one** of many routine laboratory practices (such as distillation, crystallization etc, see below) for the purification/isolation of the desired products. The various claims limitations of impurity in the sample of the impure fentanyl preparation (claims 1, 14-21), determining loading ratio (claim 3), various stationary silanized silicagel solid supports (claims 4-6), mobile phases (claims 11-13, 22, 23), doping acids for maintaining pH (claim 26), column packing, selecting solvents (claims 22, 23), collecting, combining and recycling (claim 25) etc, are recitations of routine operating chromatographic procedures and protocols

well known in the art of organic laboratory practice. The various references cited by the Examiner are illustrations of the reverse-phase hplc procedures as applied to various types of molecules (see the difference structures in the previous office action) for purification by routine variations of the instant claim limitations. Reiterating that the instant hplc **process** is **new** and the substrate being purified are different does not make a routine laboratory procedure **new**. As previously quoted MPEP states that "[w]here the general conditions of a claim are disclosed in the prior art, it is **not inventive** to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Contrary to Applicants remarks, as stated in the previous office action (see page 8, of papers filed 11/21/2008), the affidavit filed 09/25/2008 was fully considered: Specifically, the inventor restates applicant's remarks. Thus items 4 and 5 of the affidavit, in effect, states that fentanyl not Lincomycin is being purified, and the details of the hplc protocols of Lincomycin are different from the instant claimed steps. Examiner has repeatedly agreed with the applicant's position on the differences in the compounds and the details of the (hplc) procedures. Item 6 of the affidavit discussed the 'mechanical' aspect of scaling up of laboratory procedures to industrial production of narcotics. Again, while it is agreed that scaling-up of a analytical method to large industrial operation is not simple multiplication of numbers such as column size etc., nothing unobvious is presented in the instant case given the routine nature of the hplc purification procedures. In item 7, applicant states that since prior to the instant

application fentanyl is purified by precipitation and crystallization procedures, one of skill in the art would not look to chromatographic methods. Absent in the affidavit, pertaining to item 7, is any comparative study of unexpected results resulting from the use of instant chromatography method over precipitation/crystallization methods. It is the Examiner's position that, HPLC method was one of many routine well known chemistry laboratory methods that were available to one of ordinary skill in the art at the time of the instant application and choosing one over the other is within the skill of laboratory technician.

The ***pending claims 1, 3-6, 8-26 are not allowable because*** a patent may not be obtained ***though the invention is not identically disclosed or described***, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole ***would have been obvious*** at the time the invention ***to one of ordinary skill*** in industrial chemistry laboratory.

#### ***Double Patenting***

Previously presented double patenting rejection is held in abeyance as per applicant's request.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NIZAL S. CHANDRAKUMAR whose telephone number is (571)272-6202. The examiner can normally be reached on 8.30 AM - 4.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571 0272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Nizal S Chandrakumar/

Examiner, Art Unit 1625